

THE SYNTHESIS OF COMPOUNDS RELATED
TO DIHYDROSPHINGOSINE

BY
HARRIET ESTHER ROCKWELL

B. S., Keuka College, 1937

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE SCHOOL OF THE
UNIVERSITY OF ILLINOIS, 1946

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INTRODUCTION

The preparation of a compound called sphingine, by catalytic reduction of crude sphingosine bases, was reported in 1916 by Levene and West¹. An apparently identical compound was also synthesized by reduction of dihydrosphingosine with hydriodic acid. This compound was identified as 2-hydroxyoctadecylamine, and it was suggested that it was formed by reduction of anhydrosphingosine, a dehydration product of sphingosine. Establishment of the structure of sphingosine² as 2-aminooctadecen-1,3-diol suggests that anhydrosphingosine could readily be formed from it by loss of the allylic 3-hydroxyl group. This would produce a diene having a primary amino group on a carbon attached to one of the double bonds, and might account for the fact that crude sphingosine tends to lose ammonia when allowed to stand as the free base. Reduction of anhydrosphingosine would form 2-aminooctadecanol.

There have recently become available in this laboratory³ salts of sphingosine base fractions from which most of the sphingosine, dihydrosphingosine, and O-methylsphingosine have been removed. These fractions should contain anhydrosphingosine in much greater concentration than any previously available. It was therefore decided to repeat Levene's preparation of sphingine by reduction of one of these fractions rich in the compound which is its probable source.

At the same time the synthesis of 2-aminooctadecanol was undertaken with two purposes in mind. Comparison of this synthetic compound with the isolated sphingine would afford further evidence for the structure of sphingosine as proposed in this laboratory. In addition, this synthesis would serve as a model for the synthesis of dihydrosphingosine, which would provide the final proof of structure of this group of compounds.

Of the several possible methods for synthesis of 1-hydroxy-2-amino compounds, the one described by Levene, et al.⁴, the reduction of the corresponding α -amino esters with Raney nickel at high pressures and slightly elevated temperatures, was chosen. This method offers possibilities for the separation of isomers before the reduction is carried out, since Levene has reported that no racemization of optically active compounds occurred during the reduction.

DISCUSSION OF RESULTS

Synthetic 2-aminooctadecanol was prepared in excellent yield by high-pressure reduction of methyl α -aminostearate, using Raney nickel as catalyst. The compound was characterized by the preparation of its sulfate, hydrochloride, and *p*-hydroxyazobenzene-*p*-sulfonate, and its diacetyl derivative. The properties of the synthetic compound and of its derivatives compared closely with those reported by Levene for sphingine, with the exception that the synthetic compound was optically inactive.

Sphingine was prepared by reduction over palladium black of the base fraction rich in anhydrosphingosine and nearly free of sphingosine, dihydrosphingosine, and O-methylsphingosine. Again, the properties of the free base, sulfate, and acetyl derivative compared closely with those of the synthetic compound. The sphingine prepared here was optically inactive. If sphingine does come from anhydrosphingosine, the product would be expected to be racemic, and it is difficult to account for Levene's report that diacetylsphingine was dextrorotatory. It is probable that his product was contaminated with dihydrosphingosine, but the optical rotation even of pure triacetyldihydrosphingosine is lower than that reported for sphingine, so this cannot be the whole explanation.

An attempt was made to prepare 2-amino-3-methoxyoctadecanol, one of the isomers of which would be O-methyldihydrosphingosine, by the reduction of methyl α -amino- β -methoxystearate. The corresponding bromostearic acid was prepared by the addition of methyl hypobromite to

2,3-octadecenoic acid. It was then aminated and esterified, but the reduction of the product yielded only a small amount of basic material.

SUMMARY

2-Aminooctadecanol, prepared by high-pressure reduction of methyl α -aminostearate, has been shown to be identical with sphingine prepared by reduction of bases rich in anhydrosphingosine and nearly free of sphingosine, dihydrosphingosine, and O-methylsphingosine. It also corresponds closely to the compound reported by Levene, except that the compounds reported here were optically inactive. This is what would be expected if sphingine is formed from anhydrosphingosine.

The identity of the synthetic aminooctadecanol with the isolated sphingine is further proof that sphingosine is 2-aminooctadecen-1,3-diol, instead of the 1,2-diol, or the 2,3-diol.

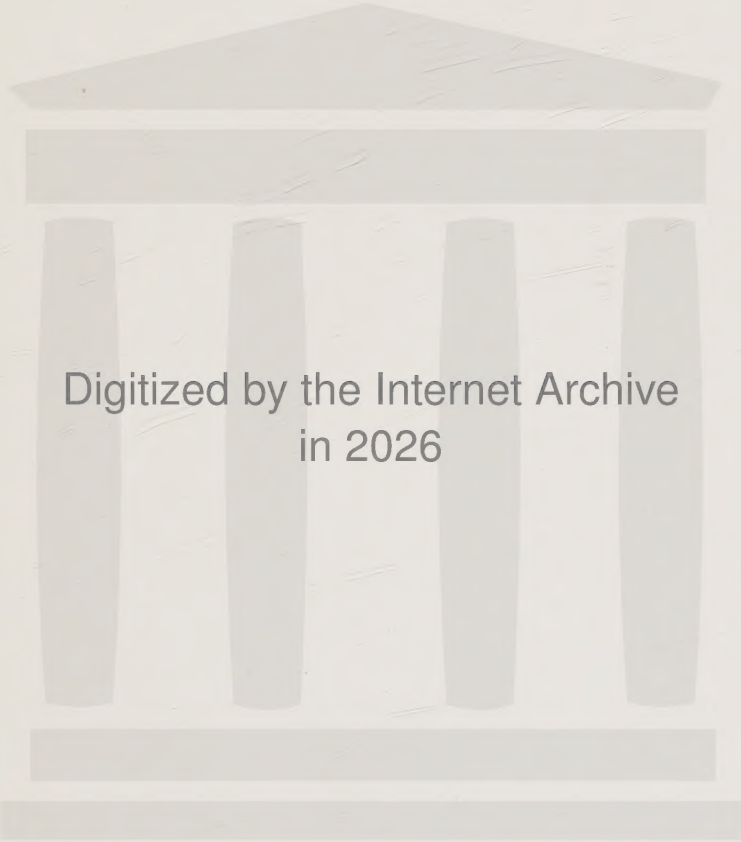
The synthesis of methyl α -amino- β -methoxystearate from stearic acid has also been described.

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VITA

The author was born on April 16, 1916, in Oneida, New York. She was graduated from Oneida High School in 1933, and entered Keuka College in the fall of that year as the holder of a New York State four year college scholarship. She received the degree of Bachelor of Science cum laude in 1937. From April, 1938, to May, 1939, she was a student in the laboratory technicians' training course at Michael Reese Hospital, Chicago, Illinois. She was employed as technician at the Madison County Bacteriological Laboratory, Oneida, New York, from June, 1939, until September, 1943, leaving this position to enter the Graduate School of the University of Illinois. In June, 1944, she was awarded a Graduate School fellowship, which she held until February, 1946.



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